

We claim:

1. A method of manipulating a microscopic quantity of material, comprising:  
providing an optical fiber probe having a tip with a hole fabricated therein, said  
hole being sufficiently small and sufficiently deep that upon immersion of said tip in said  
material a virtual seal forms to inhibit penetration of said material into said hole;  
5 immersing said tip in said material; and  
sending laser radiation through said optical fiber probe to disrupt said virtual seal  
and thereby promote entry of said material into said hole.
2. A method as claimed in claim 1, wherein said tip is sharp to facilitate penetration  
10 of said probe into a medium containing said material.
3. A method as claimed in claim 2, wherein said laser radiation is pulsed.
4. A method as claimed in claim 1, wherein said hole has a diameter of between 10-  
200 nm.
5. A method as claimed in claim 2, wherein said sharp tip has a conical structure.
- 15 6. A method as claimed in claim 1, wherein said hole has an aspect ratio of at least  
1:1.
7. A method as claimed in claim 6, wherein said hole has a diameter of less than 200  
nm.
8. A method as claimed in claim 1, wherein said optical fiber probe forms part of an  
20 array of such probes.
9. A method as claimed in claim 8, wherein said array of probes are integrally  
formed within a common substrate.

10. A method as claimed in claim 9 wherein said array of probes are interfaced with a biochip.
11. A method wherein a cw laser beam with an annular light intensity profile produced at said tip is applied to said optical fiber to trap in three dimensions a particle or  
5 biological material in a liquid near the probe tip.
12. A method as claimed in claim 1, wherein a pulsed laser beam is applied to trap the said material to perform a biopsy.
13. A method as claimed in claim 1 wherein said probe is used to promote the entry of a bead containing a drug or a sensor into the hole for ejection into a biological material .
- 10 14. A method as claimed in claim 1, wherein material trapped in the hole is injected into a mass spectrometer for constituent analysis.
15. A method as claimed in claim 1, wherein material in said hole is subsequently controllably ejected with the aid of a pulsed laser beam.
16. A method as claimed in claim 15, wherein said ejected material is ejected into a  
15 living cell.
17. A probe for manipulating small quantities of material, comprising:  
an optical fiber having a tip with a hole fabricated therein, said hole being sufficiently small and sufficiently deep that upon immersion of said tip in said material a virtual seal forms to inhibit penetration of said material into said hole; and  
20 said optical fiber probe providing a waveguide to direct laser radiation to said hole to disrupt said virtual seal and thereby promote entry of said material into said hole.

18. A probe as claimed in claim 17, wherein said tip is sharp to facilitate penetration of said probe into a medium containing said material.
19. A probe as claimed in claim 17, wherein said hole has an aspect ratio of at least 1:1.
- 5 20. A probe as claimed in claim 19, wherein said hole has a diameter of 10-200 nm.
21. A probe as claimed in claim 17, wherein said sharp tip is in the form of a conical structure and said hole is provided on the apex of said conical structure.
22. A probe as claimed in claim 17, wherein the waveguide region surrounding said hole is annular and has a width close to  $\lambda/2n$ , where  $n$  is the refractive index of the
- 10 waveguide medium surrounding the hole and  $\lambda$  is the wavelength of the laser radiation.
23. A probe as claimed in claim 18, wherein the optical fiber has a portion of reduced diameter adjacent to said sharp tip.
24. A probe as claimed in claim 17, wherein said optical fiber has a high GeO<sub>2</sub> doped core.
- 15 25. A probe as claimed in claim 24, wherein said optical fiber has an F<sub>2</sub> doped cladding.
26. A probe as claimed in claim 17, wherein said optical fiber has an index of refraction which is approximately parabolic in shape across said core.
27. A probe as claimed in claim 26, wherein said index of refraction has a narrow
- 20 central dip in said core that drops approximately to the level of the cladding.
28. A method of making a probe for manipulating small quantities of material, comprising:

forming a tip at the end of an optical fiber providing a waveguide to direct a laser pulse thereto; and

forming a hole in said tip, said hole being sufficiently small that upon immersion of said tip in said material a virtual seal forms to inhibit penetration of said material into  
5 said hole.

29. A method as claimed in claim 28, wherein said tip is sharp to facilitate penetration of said probe into a medium containing said material.

30. A method as claimed in claim 29, wherein said optical fiber has a cladding and a core, said optical fiber is selectively etched to produce said sharp tip with a hole.

10 31. A method as claimed in claim 28, wherein said optical fiber is a high GeO<sub>2</sub> doped single mode fiber.

32. A method as claimed in claim 28, wherein said optical fiber has an index of refraction which is approximately parabolic in shape across said core.

15 33. A method as claimed in claim 31, wherein the cladding of said optical fiber is F<sub>2</sub> doped.

34. A method as claimed in claim 28, wherein said optical fiber is selectively etched with a buffered oxide etchant.

35. A method as claimed in claim 34, wherein prior to said selective etching said optical fiber is etched to reduce the optical fiber diameter at least in a portion adjacent  
20 said tip.

36. A method as claimed in claim 28, wherein a flat-topped conical structure is first formed at an end of the optical fiber, and then a focused ion beam is employed to drill a hole into the top of the conical structure.

37. A method as claimed in claim 36, wherein said optical fiber is an outside vapor deposition, high GeO<sub>2</sub> doped single-mode fiber, and said single-mode fiber is chemically etched to produce said flat-topped conical structure.

38. A method as claimed in claim 37, wherein said conical structure is metalized then modified with a FIB to produce an annular light intensity distribution around said hole when light is sent through the fiber probe.

39. A method as claimed in claim 38, wherein said probe is used to trap an external particle or biological object close to the end of the tip.

40. A method as claimed in claim 36, wherein said flat-topped conical structure is formed on a hemispherical end of said optical fiber.

41. A method of inserting a small quantity of material into a cell, comprising:  
immersing in said material an optical fiber probe having a tip with a hole fabricated therein, said hole being sufficiently small that upon immersion of said tip in said material a virtual seal forms to inhibit penetration of said material into said hole;  
sending laser pulse radiation said optical fiber probe to disrupt said virtual seal and thereby promote entry of said material into said hole;  
inserting said optical fiber probe into said cell; and  
ejecting said material from said probe into said cell.

42. A method as claimed in claim 41, wherein a pulsed laser beam is applied to said material trapped in said hole to eject said material therefrom.

43. An apparatus for analyzing microscopic quantities of material comprising:

a substrate;

an array of waveguides formed in said substrate, each said waveguide terminating in a hole sufficiently small and sufficiently deep that upon immersion thereof in said

5 material a virtual seal forms to inhibit penetration of said material into said hole;

a laser arranged to send laser pulse radiation through said waveguides to disrupt said virtual seal and thereby promote entry of said material into said holes.

44. An apparatus as claimed in claim 43, wherein said substrate forms part of a biochip.

10 45. A method of loading a bead containing a drug or a sensor for ejection into a biological material, comprising:

providing an optical fiber probe having a tip with a hole fabricated therein, which can be partially filled with a fluid;

placing a bead with a size matched to the hole to seal the hole entrance; and

15 then sending laser radiation through the probe to heat the fluid to disrupt the said seal and thereby promote entry of said bead into said material.

46. A method as claimed in claim 45, wherein said seal is disrupted by sending a laser pulse or pulses through said optical fiber probe.

47. A method as claimed in 45 wherein said hole is metalized to absorb the laser  
20 radiation to rapidly heat the fluid to disrupt the seal.

48. A method of making an optical probe, comprising:

providing an optical fiber probe having a sharp substantially conical tip;

coating said tip with a thin metal layer;

drilling a microscopic hole in through said metal layer into said conical tip using a focused ion beam to provide a reservoir for optical sampling of material placed in said hole.

49. A method as claimed in claim 48, wherein said conical tip is made of silica.

5 50. A method as claimed in claim 48, wherein said focused ion beam is used to selectively drill a hole through just said thin metal layer to make an ultra-small hole for zeptoliter optical sampling of single-molecules.

51. A method of making a probe for manipulating microscopic quantities of material, comprising:

10 providing an optical fiber probe having a sharp tip;  
coating said tip with a thin layer of metal  
drilling a microscopic hole in through said metal layer into said tip;  
removing the thin metal layer; and  
coating at least the inside of said hole with malleable metal.

15 52. A method as claimed in claim 51, wherein the outer surface of the tip is also coated with metal, and further comprising the step of removing the metal from the top of the tip of the probe while retaining metal in the hole so as to create an annular-shaped light distribution in the vicinity of said tip for the light trapping of an external particle adjacent said tip.

20 53. A method as claimed in claim 52, wherein said metal is removed from said top of the tip by pressing said probe on a flat smooth surface in a controlled fashion.

54. A method as claimed in claim 52, wherein said tip is conical.

55. A method as claimed in claim 51, wherein said hole is formed by selective etching.

56. A method as claimed in claim 51, wherein said hole is formed with the aid of a focused ion beam.

5 57. A method as claimed in claim 51, wherein said metal-coated hole provides a metalized reservoir which absorbs laser radiation sent down the fiber for material extraction or ejection into or from said metal coated hole, respectively.

58. A method as claimed in claim 51, wherein only the inside of said hole is coated with metal which absorbs laser radiation sent through the fiber to provide a sub-micron  
10 sized laser controlled fiber nanoheater.